

wherein said filamentous bacteriophage particles display on their surface a polypeptide which is a specific binding pair member capable of binding a complementary ligand, and each filamentous bacteriophage particle contains genetic material including nucleic acid encoding said polypeptide, which nucleic acid encoding the polypeptide is provided by mutation of nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof, wherein said enzyme or fragment thereof is a non-immunoglobulin protein, which said enzyme or fragment thereof is able to bind a ligand of said enzyme and is at least 200 amino acids,

wherein said filamentous bacteriophage particles display a population of specific binding pair members, and

separating particles displaying specific binding pair members which have a desired enzymatic activity.

REMARKS

In response to the Advisory Action of March 24, 2003, the Applicants have amended claims 78, 80, 82 and 84 to include the limitations "wherein said enzyme or fragment thereof non-immunoglobulin protein" making the claim consistent with the allowed claim 145 and its dependents. Attorney for applicants believe that the application is in condition for allowance. Favorable consideration is respectfully requested. Therefore, applicants believe that the application is in condition for allowance.

The Examiner indicates in Paragraph No. 5 of the Advisory Action of March 24, 2003 that the Information Disclosure Statement filed on March 13, 2003 failed to comply with 37 CFR 1.97 because it lacked the fee set forth in 37 C.F.R. § 1.117(p). The Information Disclosure Statement signed and submitted to the U.S. Patent & Trademark Office on March 13, 2003 included a paragraph authorizing the Commissioner to charge any deficient fees to the Deposit

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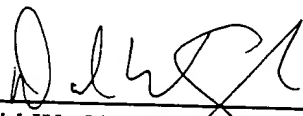
Account of Katten Muchin Zavis Rosenman, No. 50-1214. The applicants believe that no petition was required for the Information Disclosure Statement signed and submitted on March 13, 2003; although a "Petition to Expunge" was submitted with the Information Disclosure Statement signed and filed on September 10, 2003 (faxed on February 6, 2003). A copy of the Petition to Expunge, our check no. 299090 submitted in the amount of \$130 for the Petition under 37 C.F.R. § 1.17(h); our cancelled check no. 299090, and a copy of the postcard stamped received by the Tech Center on September 11, 2003 are also enclosed.

The Examiner is invited to contact the undersigned with any questions, comments or suggestions relating to the referenced patent application.

The Commissioner is hereby authorized to charge any additional fees which may be required in this application under 37 C.F.R. §§1.16-1.17 during its entire pendency, or credit any overpayment, to Deposit Account No. 50-1214. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-1214.

Respectfully submitted,

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APPENDIX OF PENDING CLAIMS

45. A method according to claim 145 wherein said enzyme or fragment is at least 200 amino acids.
46. A method according to claim 145 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
47. A method according to claim 45 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
48. A method according to claim 145 wherein particles formed by said expression are selected or screened to provide an individual displayed polypeptide specific binding pair member or a mixed population of displayed polypeptide specific binding pair members associated in respective particles with nucleic acid encoding said displayed polypeptide specific binding pair member or specific binding pair members, the specific binding pair member or specific binding pair members thus provided having ability to bind a complementary ligand.
49. A method according to claim 48 wherein the particles are selected by affinity with a complementary ligand.
50. A method according to claim 49 which comprises recovering any particles bound to said complementary ligand by washing with an eluant.
51. A method according to claim 50 wherein the eluant contains a molecule which competes with said particles for binding to said complementary ligand.
52. A method according to claim 49 wherein the particles are applied to said complementary ligand in the presence of a molecule which competes with said particles for binding to said complementary ligand.
53. A method according to claim 48 wherein the particles are selected by enzymatic activity of the displayed polypeptide.
54. A method of producing a specific binding pair member, the method comprising:
 - (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48; and
 - (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
55. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48; and
 - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
56. A method of producing a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49; and
 - (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
57. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49; and
 - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
58. A method of producing a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53; and
 - (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
59. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53; and
 - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
60. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and
 - (ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

61. A method of producing a specific binding pair member, the method comprising:
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 60, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
62. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).
63. A method of producing a specific binding pair member, the method comprising:
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 62, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
64. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).
65. A method of producing a specific binding pair member, the method comprising:
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 64, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.

78. A method of producing a member of a specific binding pair, the method comprising:
contacting a library of filamentous bacteriophage particles with a desired ligand,
wherein said filamentous bacteriophage particles display on their surface a
polypeptide which is a specific binding pair member capable of binding a
complementary ligand, and each filamentous bacteriophage particle contains genetic
material including nucleic acid encoding said polypeptide, which nucleic acid
encoding the polypeptide is provided by mutation of nucleic acid encoding a specific
binding pair member which comprises an enzyme or fragment thereof, wherein
said enzyme or fragment thereof is a non-immunoglobulin protein, which said
enzyme or fragment thereof is able to bind a ligand of said enzyme and is at least
100 amino acids,
- wherein said filamentous bacteriophage particles display a population of specific
binding pair members, and
- separating particles displaying specific binding pair members which bind to said
desired ligand.
79. A method according to claim 78 wherein said polypeptide is displayed as a fusion with a
gene III capsid protein surface component of phage fd or its counterpart in another
filamentous phage.
80. A method of producing a member of a specific binding pair, the method comprising:
contacting a library of filamentous bacteriophage particles with a desired ligand,
wherein said filamentous bacteriophage particles display on their surface a
polypeptide which is a specific binding pair member capable of binding a
complementary ligand, and each filamentous bacteriophage particle contains genetic
material including said nucleic acid encoding said polypeptide, which nucleic acid
encoding the polypeptide is provided by mutation of nucleic acid encoding a specific
binding pair member which comprises an enzyme or fragment thereof, wherein said
enzyme or fragment thereof is a non-immunoglobulin protein, which said
enzyme or fragment thereof is able to bind a ligand of said enzyme and is at least 100
amino acids,
- wherein said filamentous bacteriophage particles display a population of specific
binding pair members, and
- separating particles displaying specific binding pair members which have a desired
enzymatic activity.
81. A method according to claim 80 wherein said polypeptide is displayed as a fusion with a
gene III capsid protein surface component of phage fd or its counterpart in another
filamentous phage.
82. A method of producing a member of a specific binding pair, the method comprising:
contacting a library of filamentous bacteriophage particles with a desired ligand,
wherein said filamentous bacteriophage particles display on their surface a

polypeptide which is a specific binding pair member capable of binding a complementary ligand, and each filamentous bacteriophage particle contains genetic material including nucleic acid encoding said polypeptide, which nucleic acid encoding the polypeptide is provided by mutation of nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof, wherein said enzyme or fragment thereof is a non-immunoglobulin protein, which said enzyme or fragment thereof is able to bind a ligand of said enzyme and is at least 200 amino acids,

wherein said filamentous bacteriophage particles display a population of specific binding pair members, and

separating particles displaying specific binding pair members which bind to said desired ligand.

83. A method according to claim 82 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
84. A method of producing a member of a specific binding pair, the method comprising:
contacting a library of filamentous bacteriophage particles with a desired ligand, wherein said filamentous bacteriophage particles display on their surface a polypeptide which is a specific binding pair member capable of binding a complementary ligand, and each filamentous bacteriophage particle contains genetic material including nucleic acid encoding said polypeptide, which nucleic acid encoding the polypeptide is provided by mutation of nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof, wherein said enzyme or fragment thereof is a non-immunoglobulin protein, which said enzyme or fragment thereof is able to bind a ligand of said enzyme and is at least 200 amino acids,
wherein said filamentous bacteriophage particles display a population of specific binding pair members, and
separating particles displaying specific binding pair members which have a desired enzymatic activity.
85. A method according to claim 84 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
86. A method of producing a specific binding pair member, the method comprising:
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78; and
(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

87. A method according to claim 86 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
88. A method of producing a specific binding pair member, the method comprising:
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80; and
(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
89. A method according to claim 88 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
90. A method of producing a specific binding pair member, the method comprising:
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82; and
(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
91. A method according to claim 90 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
92. A method of producing a specific binding pair member, the method comprising:
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84; and
(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
93. A method according to claim 92 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
94. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78; and
(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

95. A method according to claim 94 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
96. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80; and
 - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
97. A method according to claim 96 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
98. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82; and
 - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
99. A method according to claim 98 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
100. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84; and
 - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
101. A method according to claim 100 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
102. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and
 - (ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair

member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

103. A method of producing a specific binding pair member, the method comprising:
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 102, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
104. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).
105. A method of producing a specific binding pair member, the method comprising:
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 104, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
106. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

107. A method of producing a specific binding pair member, the method comprising:
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 106, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
108. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).
109. A method of producing a specific binding pair member, the method comprising:
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 108 wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
145. A method of producing a specific binding pair member, which method comprises:
expressing in recombinant host cells a library of nucleic acid sequences encoding a genetically diverse population of polypeptides, which library of nucleic acid sequences is provided by mutating nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof wherein said enzyme or fragment thereof is a non-immunoglobulin protein, which enzyme or fragment thereof is able to bind a ligand of said enzyme and is at least 100 amino acids,
wherein said polypeptides encoded by the library are displayed at the surface of filamentous bacteriophage particles, and wherein genetic material of each filamentous bacteriophage particle displaying a polypeptide includes nucleic acid